PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

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02 JUN 2004
FILE No. 01/22939
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PCT

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

Applicant's or agent's file reference 0122939	Date of Mailing *(day/month/year)* 21 MAY 2004 **PAYMENT DUE** within 15 days from the above date of mailing
International application No. PCT/US02/90230	International filing date *(day/month/year)* 05 March 2002 (05.03.2002)
Applicant YISSUM RESEARCH DEVELOPMENT COMPANY OF THE HEBREW	

1. This International Searching Authority

(i) considers that there are 18 *(number of)* inventions claimed in the international application covered by the claims indicated below/on an extra sheet:
Please See Continuation Sheet

and it considers that **the international application does not comply with the requirements of unity of invention** (Rules 13.1, 13.2 and 13.3) for the reasons indicated below/on an extra sheet:
Please See Continuation Sheet

(ii) ☐ has carried out a partial international search (see Annex) ☒ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.: 1-45, including SEQ ID NO:1 and SEQ ID NO:2

(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid.

2. The applicant is hereby **invited**, within the time limit indicated above, to pay the amount indicated below:

$210.00	X 17	= $3,570.00
Fee additional per invention	number of additional inventions	total amount of additional fees

The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest,** i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. ☒ Claim(s) Nos. 104 have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer Stuart F. Baum Janice Fogel for Telephone No. 703-308-0196

Form PCT/ISA/206 (July 1992)

INVITATION TO PAY ADDITIONAL FEES

International application No.
PCT/US02/90230

This International Search Authority has found 18 inventions claimed in the International Application covered by the claims indicated below:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-45, drawn to an isolated nucleic acid comprising a first polynucleotide encoding a boiling stable protein, or a detergent stable protein or a protease resistant protein and a second polynucleotide comprising a promoter operably linked to the first polynucleotide or wherein the first polynucleotide has a 60% sequence identity with SEQ ID NO:1, and wherein said stable protein has a sequence at least 60% identical to SEQ ID NO:2 and a method of isolating a nucleic acid encoding a boiling stable protein, or a detergent stable protein or a protease resistant protein comprising screening an expression library.

Group II, claim(s) 1-45, drawn to an isolated nucleic acid comprising a first polynucleotide encoding a boiling stable protein, or a detergent stable protein or a protease resistant protein and a second polynucleotide comprising a promoter operably linked to the first polynucleotide or wherein the first polynucleotide has a 60% sequence identity with SEQ ID NO: 5, 6, 34, 39, or 40 and wherein said stable protein has a sequence at least 60% identical to SEQ ID NO:2 or 35 and a method of isolating a nucleic acid encoding a boiling stable protein, or a detergent stable protein or a protease resistant protein comprising screening an expression library.

IF APPLICANT ELECTS GROUP II, APPLICANT IS ALSO TO ELECT ONE NUCLEIC ACID SEQUENCE AND ONE CORRESPONDING AMINO ACID SEQUENCE AS RECITED IN GROUP I. APPLICANTS HAVE THE OPTION TO PAY AN ADDITIONAL $210.00 FOR EACH ADDITIONAL PAIR OF DNA AND AMINO ACID SEQUENCES.

Group III, claim(s) 46-50, 53-60, 63-70, 73-75 and 100-102 drawn to an isolated boiling stable, detergent stable or protease resistant polypeptide and a method of preventing an aggregating protein from aggregating comprising the elected polypeptide.

IF APPLICANT ELECTS GROUP III, APPLICANT IS ALSO TO ELECT ONE NUCLEIC ACID SEQUENCE AND ONE CORRESPONDING AMINO ACID SEQUENCE FROM THE BELOW LIST:

SEQ ID NO:1; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:34; SEQ ID NO:39; SEQ ID NO:40; SEQ ID NO:2; SEQ ID NO:35.

APPLICANTS HAVE THE OPTION TO PAY AN ADDITIONAL $210.00 FOR EACH ADDITIONAL PAIR OF DNA AND AMINO ACID SEQUENCES.

Group IV, claim(s) 51-52, 61-62, 71-72, drawn to an antibody.

Group V, claim(s) 76-77, and 103 drawn to a method of enriching or isolating a denaturant stable and/or protease resistant protein having chaperone-like activity.

Group VI, claim(s) 78-79, drawn to a method of isolating a gene encoding a denaturant stable and/or protease resistant protein having chaperone-like activity comprising microsequencing a protein, designing oligonucleotides and screening a library.

Group VII, claim(s) 80, drawn to a method of isolating a nucleic acid potentially encoding a denaturant stable and/or protease resistant protein comprising screening a cDNA or genomic library with a polynucleotide comprising at least 17 bases at least 60% identical to SEQ ID NO:1, 5, 6, 34, 39, 40.

IF APPLICANT ELECTS GROUP VII, APPLICANT IS ALSO TO ELECT ONE NUCLEIC ACID SEQUENCE AS RECITED IN GROUP VII.

APPLICANTS HAVE THE OPTION TO PAY AN ADDITIONAL $210.00 FOR EACH ADDITIONAL DNA SEQUENCE.

Group VIII, claim(s) 81, drawn to a method of isolating a nucleic acid potentially encoding a denaturant stable and/or protease resistant protein comprising searching an electronic library.

IF APPLICANT ELECTS GROUP VIII, APPLICANT IS ALSO TO ELECT ONE NUCLEIC ACID SEQUENCE FROM THE BELOW LIST:

SEQ ID NO:1; SEQ ID NO:2; SEQ ID NO:5-35; SEQ ID NO:39-40.

APPLICANTS HAVE THE OPTION TO PAY AN ADDITIONAL $210.00 FOR EACH ADDITIONAL DNA SEQUENCE.

Group IX, claim(s) 82, drawn to a method of isolating a nucleic acid potentially encoding a denaturant stable and/or protease resistant protein comprising using PCR.

IF APPLICANT ELECTS GROUP IX, APPLICANT IS ALSO TO ELECT ONE NUCLEIC ACID SEQUENCE FROM THE BELOW LIST:

SEQ ID NO:1; SEQ ID NO:2; SEQ ID NO:5-35; SEQ ID NO:39-40.

APPLICANTS HAVE THE OPTION TO PAY AN ADDITIONAL $210.00 FOR EACH ADDITIONAL DNA SEQUENCE.

Group X, claim(s) 83, drawn to a method of detergent-free isolation of a protease-resistant protein.

Group XI, claim(s) 84-88, drawn to a fusion protein comprising a denaturant stable and/or protease resistant polypeptide and a method of immunization.

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Group XII, claim(s) 89-90, drawn to a method of protecting an enzyme preparation from reduction in enzymatic activity.

Group XIII, claim(s) 91, drawn to a method of administering to an animal having an immune system a polypeptide.

Group XIV, claim(s) 92-94, drawn to a method of rendering a plant more tolerant to a biotic or abiotic stress and a transgenic plant, both of which, comprising expressing a denaturant stable and/or protease resistant protein.

Group XV, claim(s) 95-99, drawn to a methods of increasing cell migration, accelerating wound healing, inducing wound healing strengthening hair, nail or skin and grooming hair, nail or skin, all of which comprising exposing or administering an amount of a denaturant stable and/or protease resistant protein.

Group XVI, claims 105-106, drawn to a method of treating a disease associated with protein aggregation of an aggregating protein.

Group XVII, claims 107-108, drawn to a method of increasing a binding avidity of a binding molecule.

Group XVIII, claims 109-113, drawn to a hetero complex comprising an oligomer including a plurality of a denaturant stable and/or protease resistant protein.

1. This International Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:
The inventions listed as Groups I through XX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Applicant is reminded that nucleotide sequences encoding different proteins each have different properties and different core structures that elicit different activities, and as such, Groups I-XVIII are not linked by, or share, a single special technical feature.

In addition the claims are not linked by a single technical feature because they are each drawn to products and processes not shared by the other. The technical feature of the isolated nucleic acid and method of isolating a nucleic acid of Group I, is not shared by the nuclei acid and method of isolating a nucleic acid of Group II, is not shared by the polypeptide and method of preventing an aggregating protein from aggregating of Group III, is not shared by the antibody of Group IV, is not shared by the method of enriching or isolating a denaturant stable and/or protease resistant protein of Group V, is not shared by the method of isolating a gene encoding a denaturant stable and/or protease resistant protein comprising microsequencing a protein, designing oligonucleotides and screening a library of Group VI, is not shared by the method of isolating a gene encoding a denaturant stable and/or protease resistant protein comprising screening a cDNA or genomic library of Group VII, is not shared by the method of isolating a nucleic acid by searching an electronic library of Group VIII, is not shared by the method of isolating a nucleic acid comprising using PCR of Group IX, is not shared by the method comprising the detergent-free isolation of a protease-resistant protein of Group X, is not shared by the fusion protein of Group XI, is not shared by the method of protecting an enzyme preparation from reduction in enzymatic activity of Group XII, is not shared by the method of administering to an animal a polypeptide of Group XIII, is not shared by the method of rendering a plant more tolerant to a biotic or abiotic stress and corresponding transgenic plant of Group XIV, is not shared by the methods of increasing cell migration, accelerating wound healing, inducing wound healing, strengthening hair, nail or skin and grooming hair, nail or skin of Group XV, is not shared by the method of treating a disease associated with protein aggregation of Group XVI, is not shared by the method of increasing a binding avidity of a binding molecule of Group XVII, or is not shared by the hetero complex of Group XVIII. Each of the recited groups do not share a special technical feature with each other.